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Army Medical Research Lab., Fort Knox, Ky. (Report No. 71)

Effect of Total Body X-Irradiation on the Plasmin Inhibitor Titer in the
Blood of Rats

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FORT KNOX, KENTUCKY

REPORT NO. 71

15 December 1951

EX COPY

EFFECT OF TOTAL BODY X-IRRADIATION ON THE PLASMIN INHIBITOR TITER IN THE BLOOD OF RATS*

*Subtask under Effects of Irradiation, AMRL project 6-59-08-013,
Subtask, Enzyme, Endocrine and Metabolism Studies in Total Body
Irradiation.

MEDICAL RESEARCH AND DEVELOPMENT BOARD
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DEPARTMENT OF THE ARMY

REPORT NO. 71

EFFECT OF TOTAL BODY X-IRRADIATION ON THE
PLASMIN INHIBITOR TITER IN THE BLOOD OF RATS*

by

Dr. Walter Kocholaty, Biochemist, William W. Ellis, Cpl and
Dr. Hans F. Jensen, Chief Biochemist

from

Army Medical Research Laboratory
Fort Knox, Kentucky
15 December 1951

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Irradiation.

Report No. 71
AMRL Project No. 6-59-08-013-S-3
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15 December 1951

ABSTRACT

EFFECT OF TOTAL BODY X-IRRADIATION ON THE PLASMIN INHIBITOR TITER IN THE BLOOD OF RATS

OBJECT

Continuing previous investigations of the mechanism of increased fibrinolysis during conditions of stress, the antifibrinolytic activity in the blood of rats was measured after ionizing irradiation and compared with the antifibrinolytic titer in starved animals.

RESULTS AND CONCLUSIONS

Exposure of rats to 1000 r total body x-irradiation produced a fall in the plasmin inhibitor titer of plasma, beginning at the second day after irradiation and then gradually increasing. Since starvation was found to exert a similar effect, no definite conclusions can be made as to the irradiation per se causing a lowering in the titer. Total body x-irradiation (1000 r) and starvation caused a weight loss of nearly identical magnitude.


RECOMMENDATIONS

Since various factors are involved in maintaining blood homeostasis, possible changes in other factors than the antiplasmin should be studied following total body x-irradiation.


Submitted by:

W. Kocholaty, Ph.D., Biochemist
W. W. Ellis, Cpl.
H. Jensen, Ph. D., Chief Biochemist

Approved by:


RAY G. DAGGS
Director of Research

Approved by:


CARL F. TESSMER
Lt. Col., M. C.
Commanding

EFFECT OF TOTAL BODY X-IRRADIATION ON THE PLASMIN INHIBITOR TITER IN THE BLOOD OF RATS

I. INTRODUCTION

It is well established that acute ionizing radiation illness is associated with pronounced hemorrhage. The equilibrium in blood between plasmin and plasmin inhibitor may be of importance in maintaining a hematic homeostasis. Any shift in the balance of these factors may be associated with either hemorrhage or thrombosis. It has been reported that a decrease in the plasmin inhibitor titer could be demonstrated in rats in "tourniquet shock" and after epinephrine administration to normal rats (1). It was of interest, therefore, to study the effect of total body x-irradiation on the plasmin inhibitor titer in blood.

II. EXPERIMENTAL

Male rats of the Sprague-Dawley strain weighing 210-325 grams were used. The animals were kept in individual cages and were weighed daily prior to and during the experiment until death or sacrifice. Three groups of animals were used:

Group I served as normal controls for Groups II and III. The animals were maintained on Purina laboratory chow and tap water.

Group II consisted of the irradiated animals. The rats were irradiated, two at a time, in a well-ventilated lucite chamber. The radiation was performed with a 250 Kv Kelly-Koett x-ray unit, the factors being: 200 Kv, 6 ma, 1/2 mm copper and 1 mm aluminum filters, target distance 29 cm. The set-up gave a dosage of 40 roentgens per minute. Each rat received either 880 r or 1000 r; 880 r was found to correspond to an LD/78 (28 days), and 1000 r to an LD/100 (8 days).

Since it is known that the food intake of irradiated animals is less than normal, it was desirable to study the effect of starvation on the plasmin inhibitor titer. In Group III food was withheld, but the animals were allowed tap water.

Animals were sacrificed on 0, 1/4, 1, 2, 3, 4, 5, and 6 days; 2 ml. of blood were drawn by direct cardiac puncture using 0.2 ml of 3.8% sodium citrate as an anticoagulant. Following centrifugation at 2800 rpm for 45 minutes, the plasma was withdrawn and used immediately or stored sealed in the refrigerator for use later the same day.

0.1 ml. of this plasma was diluted 1:40 with pH 7.25 imidazole* buffer. 0.1 ml. of this solution was allowed to react with 0.1 ml. standard trypsin**, giving a clot dissolution time of 120 seconds for 30 minutes at 25°C; the tube was then transferred to a 37.5°C bath and 0.1 ml. thrombin*** (10 units) and 0.2 ml. bovine fibrinogen**** were added. The end point as determined by bubble rise in the lysed clot was read in seconds. These were converted into units of plasmin inhibitor from a standard curve (1).

III. RESULTS

The results of the above described experiments are discussed on the basis of the effect of total body x-irradiation and starvation on the antiplasmin titer, weight and mortality.

As can be seen from Figure 1, the antiplasmin titer of the irradiated (1000 r) rats started to decrease at 2 days after irradiation, reaching a minimum at 4 days and then increased slightly at 5 and 6 days. Starvation produced a somewhat similar lowering reaching a minimal value at 6 days.

As can be seen from Figure 2, irradiated (880 r and 1000 r) and starved animals lost weight at the same rate through the seventh day. In the group receiving 880 r, the survivors (about 50%) slowly regained weight from the fifth day.

It is interesting to note that although the mortality differed greatly among the three groups, the weight loss up to five days is very nearly identical (see Figures 2 and 3).

IV. CONCLUSIONS

Exposure of rats to 1000 r total body x-irradiation produced a fall in the plasmin inhibitor titer of plasma, beginning at the second day after irradiation and then gradually increasing. Since starvation was found to exert a similar effect, no definite conclusions can be made as to whether irradiation per se caused a lowering in the titer.

* Obtained from the Edcan Laboratories, Norwalk, Conn.

** Obtained from Worthington Biochemical Laboratories, Freehold, N. J.

*** Obtained from Parke-Davis Co., Detroit, Michigan.

**** Fibrinogen prepared according to Reference (2). Concentration in the 0.5 ml. standard clot = 500 gamma, or 0.1%.

Total body x-irradiation (1000 r) and starvation caused a weight loss of nearly identical magnitude.

V. RECOMMENDATIONS

Since various factors are involved in maintaining blood homeostasis, possible changes in other factors than the antiplasmin should be studied following total body x-irradiation.

VI. BIBLIOGRAPHY

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2. Ware, A. G., M. M. Guest, and W. H. Seegers. Fibrinogen: with special reference to its preparation and certain properties of the product. *Arch. Biochem.* 13: 231, 1947.

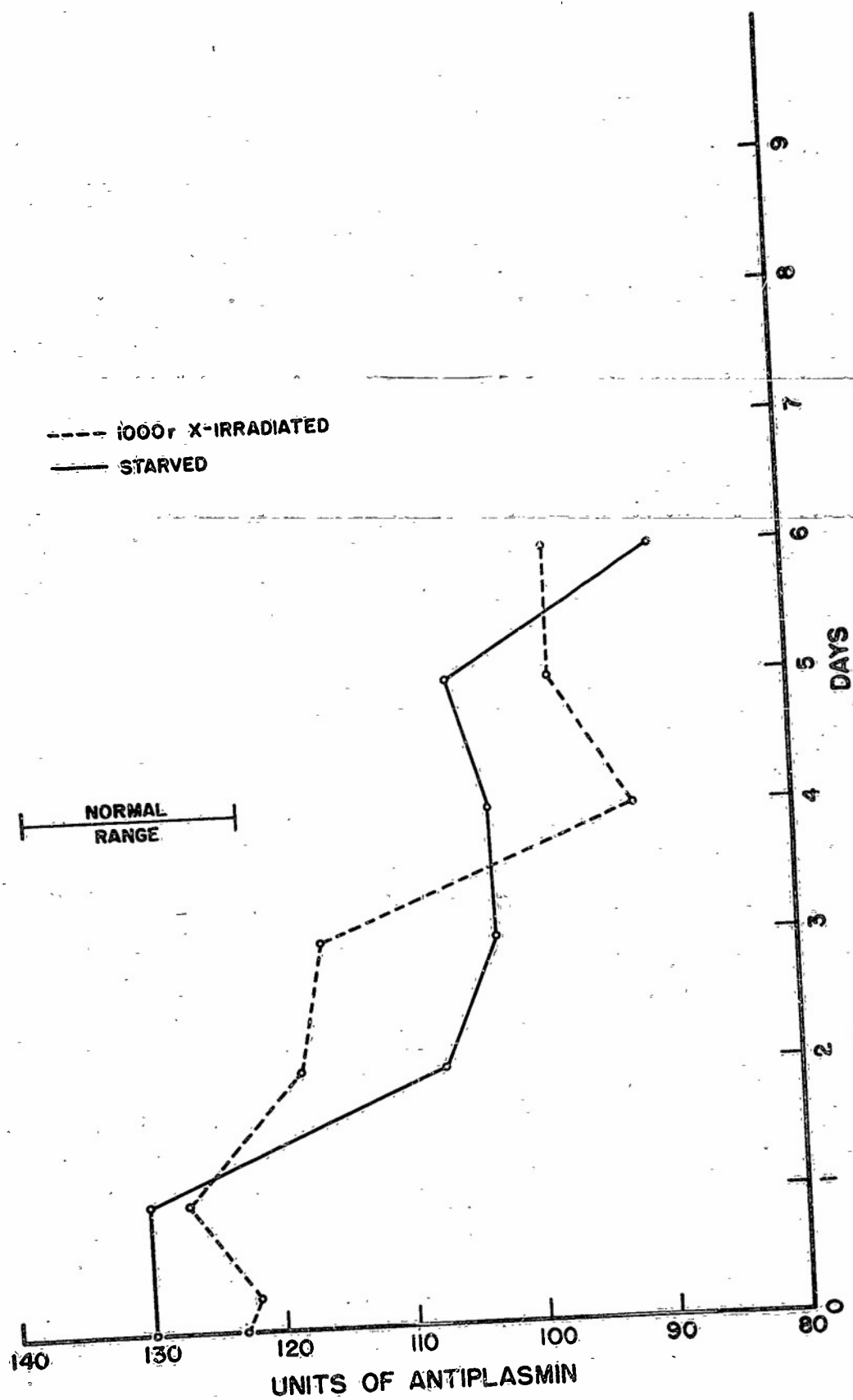


FIG. 1 CHANGE IN ANTIPLASMIN TITER FOLLOWING X-IRRADIATION AND STARVATION.

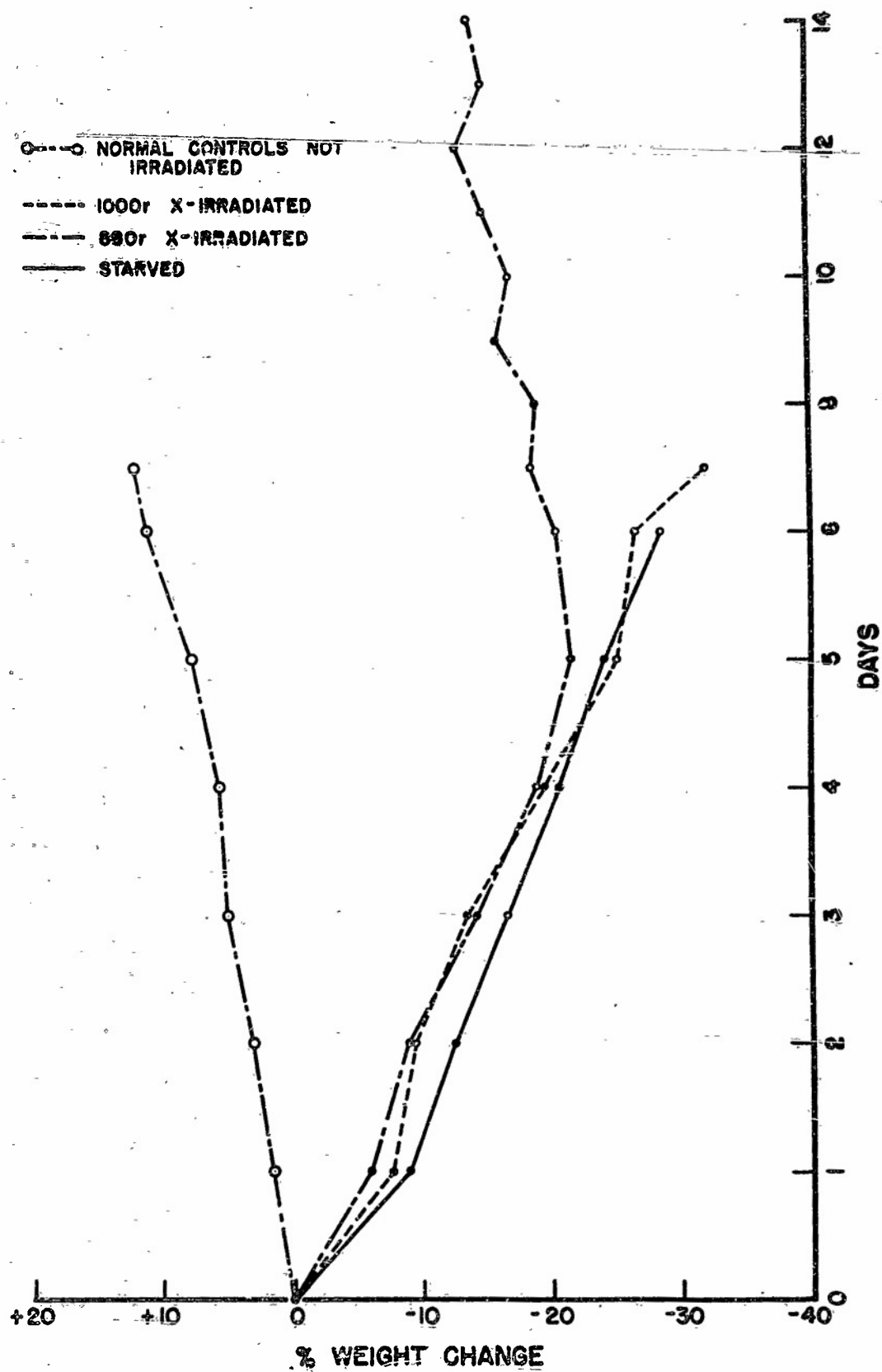


FIG. 2 CHANGE IN WEIGHT FOLLOWING X-IRRADIATION AND STARVATION.

--- 1000r X-IRRADIATED
--- 650r X-IRRADIATED
STARVED RATS - NO MORTALITY IN 8 DAYS

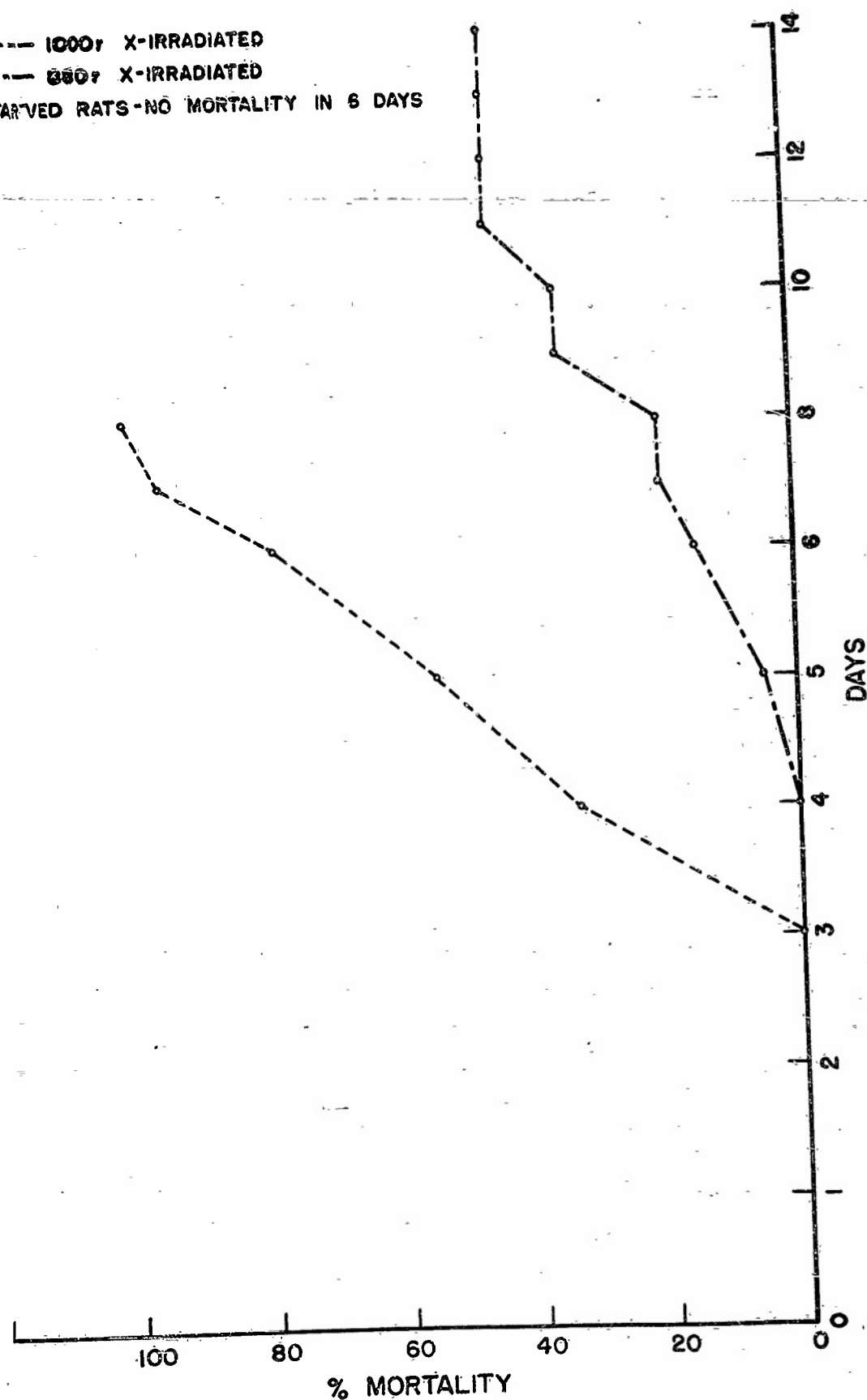


FIG. 3 MORTALITY FOLLOWING X-IRRADIATION.